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A young male patient with persistent fever due to tuberculous peritonitis

結核性腹膜炎引起頑固性發燒的青年男性患者

Tuberculous peritonitis is an uncommon disease in Hong Kong. We report a case of tuberculous peritonitis in a young male. The patient presented with persistent fever and intermittent cough for 1 month, but had no gastrointestinal symptoms. It was only through detection of slight abdominal ascites that subsequent abdominal paracentesis and laparoscopic biopsy confirmed the diagnosis. Appropriate anti-tuberculous treatment was prescribed. Progress was complicated by persistent fever and liver function derangement, successfully managed by careful titration of antituberculous medications.

在香港結核性腹膜炎是一種較少見的疾病。我們報告了一青年男性的結核性腹膜炎病例。患者呈現持久頑固的發燒和間斷咳嗽一個月，但無腸胃症狀。只有通過輕微的腹部腹水的發現，後來的腹部穿刺術和腹腔鏡活組織檢查才證實了這診斷。期後對患者進行了適當的抗結核治療。持續頑固的發燒和肝功能紊亂使病情發展複雜化，但小心使用抗結核藥物的滴定成功地控制了病情。

Introduction

It has been reported that up to 5% of patients with tuberculosis (TB) may have abdominal disease. Of these, 25% to 60% may have peritoneal involvement.[1] Concomitant active pulmonary TB associated with abdominal TB has been reported to range from 20% to 50%.[1,2] Peritoneal TB can originate from mesenteric lymph nodes, or through haematogenous spread. Symptoms are usually insidious, with abdominal swelling, fever, night sweats, anorexia, weight loss, and abdominal pain.[3] These typical symptoms may be absent, however. Clinicians should maintain a high index of suspicion for TB peritonitis, since missing the diagnosis can result in significant morbidity and potential mortality.[4,5]

Case report

A 22-year-old Chinese male was referred to the Department of Medicine and Geriatrics at Our Lady of Maryknoll Hospital by his family physician in May 1999 for symptoms of persistent fever and chills, together with intermittent cough for 1 month. Chest X-ray showed no abnormality. There had been no significant past medical or drug history. The patient also denied any history of substance or drug misuse, or multiple sexual partners.

The patient worked as a salesman and travelled to China most weeks. There were no gastrointestinal complaints, such as abdominal pain or bowel irregularity. The patient reported that he had lost approximately

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10 kg over the month of his illness. Private practitioners had prescribed various cough medications and antibiotics, which had had no effect on the patient's symptoms.

On initial examination the patient was febrile, with a temperature of 37.8°C. There was no jaundice, cyanosis, or pallor. Chest examination showed no abnormal signs and there was no palpable lymphadenopathy. Cardiac examination was normal, with no detectable murmur. Abdominal examination revealed no mass, organomegaly, or free fluid on admission. Rectal examination showed the presence of soft yellow stool, with no mass detected. Neurological examination was unremarkable. No rash or skin lesion was detected. There was no sign of joint inflammation or arthritis. Fundal examination was normal. The patient was thus investigated for pyrexia of unknown origin.

The results of the investigation showed a haemoglobin level of 108 g/L (normal range, 140-180 g/L), a mean corpuscular volume of 81.2 fL (normal range, 76-100 fL), a white blood cell (WBC) count of 5.5 x 10^9/L (normal range, 3.2-9.8 x 10^9/L), a platelet count of 338 x 10^9/L, (normal range, 150-450 x 10^9/L), and an erythrocyte sedimentation rate of 56 mm/h (normal range, 0-20 mm/h). Renal function tests (RFT) were normal, as was urine analysis. Liver function tests revealed slightly increasing levels of alkaline phosphatase (ALP) of 153 U/L (normal range, 30-120 U/L), and γ-glutamyl transpeptidase of 162 U/L (normal range, 0-30 U/L). Chest X-ray showed clear lung fields. Blood, mid-stream urine, stool, and sputum cultures were all negative. The cold agglutinin test for atypical pneumonia was negative. Hepatitis B surface antigen testing was negative. Stool tests for parasites, including amoeba, were negative. Thick and thin blood films were negative for malarial parasites. Antinuclear factor, the Widal test, Weil-Felix test, Monospot test, influenza A rapid test, and human immunodeficiency virus antibody test were all negative. Serum brucella and leptospira titres were normal. Ultrasound of the abdomen revealed a normal liver echo, and the common bile duct, portal vein, and spleen were not enlarged. The gall bladder was normal, with no stones, and the pancreas and kidneys were unremarkable. A small amount of ascitic fluid was noted, however.

The patient continued to be febrile, with temperatures of up to 40°C despite initial oral erythromycin therapy given empirically, for possible atypical pneumonia. In the few days after admission, the patient's abdominal distension was more noticeable and ascites could be clinically detected. Ultrasound-guided aspiration of the ascites was performed and 25 mL of straw-coloured fluid was obtained. The ascitic fluid cell count showed a red blood cell count of 0.02 x 10^{12}/L, and a WBC count of 3 x 10^9/L, of which 8% were polymorphs and 92% were mononuclear cells. Biochemistry testing of the ascitic fluid revealed a glucose level of 2.5 mmol/L, and a protein level of 10 g/L. Simultaneous plasma glucose was 6.5 mmol/L. A laparoscopic examination performed under general anaesthesia revealed a moderate amount of turbid peritoneal fluid. The peritoneum was inflamed, with multiple small white seedings. The small bowel visualised was matted, with adhesions between the small bowel and peritoneum, together with multiple small seedings on the serosa (Figs 1 and 2). These seedings were subsequently examined by biopsy.

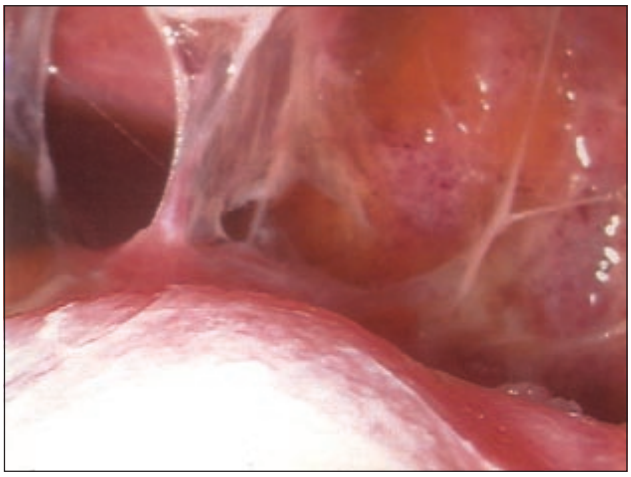

Fig 1. Laparoscopic view of the abdominal cavity showing adhesions between bowel and peritoneum

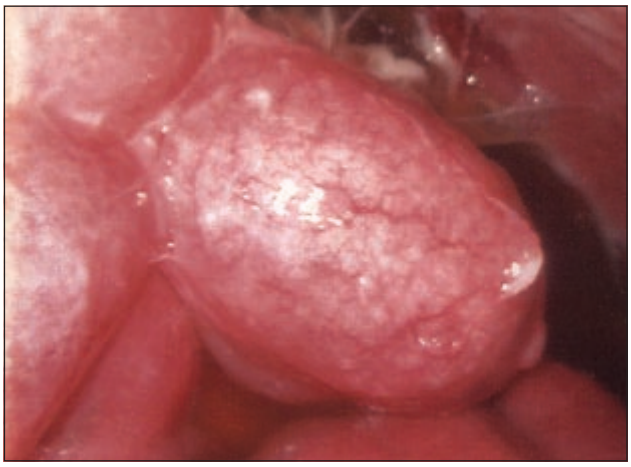

Fig 2. Laparoscopic view of the abdominal cavity showing matted small bowel and adhesions between the small bowel and peritoneum

At this stage, the diagnosis of TB peritonitis was made. The patient was given the following anti-TB medications in the appropriate dosages: isoniazid

(INAH), rifampicin (RMP), ethambutol (EMB), pyrazinamide, and pyridoxine (B6).[6] His fever subsided 4 days after initiation of treatment. Although peritoneal fluid and sputum smears for acid-fast bacilli (AFB) were negative, the peritoneal biopsy revealed many tuberculoid granulomas, with positive Ziehl-Neelsen staining for AFB. The diagnosis of TB peritonitis was thus confirmed. The patient was discharged on appropriate medications after resolution of his fever and cough, with follow-up in the specialist outpatient clinic planned.

The patient was readmitted 5 days later with recurrence of fever, (temperatures of up to 39°C), and chills. His chest was clear on examination. The abdomen remained slightly distended. Complete blood count revealed a WBC count of 7.1 x 10^9/L. Erythrocyte sedimentation rate remained at 52 mm/hr, and RFTs were normal. Alkaline phosphatase was slightly elevated to 139 U/L (normal range, 30-120 U/L). Repeat abdominal ultrasound revealed a loculated effusion of 5 x 5 x 3 cm, inferior to the right lobe of the liver, together with fibrous strands inside. Abscess formation was suspected. Paracentesis was performed, with only 90 ml of straw-coloured fluid drained from the right infrahepatic region. There was no pus detected. Fluid for biochemistry showed a glucose level of 2.9 mmol/L, a protein level of 54 g/L, and a WBC count of 1.22 x 10^9/L, of which 97% were monocytes and 3% were polymorphs. Peritoneal fluid for AFB smear, gram stain and culture for bacteria were all negative. As no abscess was found, the fever was attributed to ongoing active tuberculosis, although the possibility of drug-induced fever could not be entirely excluded. In view of the serious infection, anti-TB drugs were continued with close monitoring of progress.

A few days later, the patient's liver function was noted to be impaired. Alanine aminotransferase was found to be 288 U/L (normal range, 0-35 U/L), aspartate aminotransferase was 567 U/L (normal range, 0-35 U/L), and ALP was 204 U/L. The initial four-drug regimen was changed to EMB, streptomycin (SM), and ofloxacin (OFL) on suspicion of drug-induced impairment in liver function.[6] The patient's liver function gradually improved during the next 2 weeks. Isoniazid, followed by RMP, was gradually re-introduced, with close monitoring of liver function. Fever eventually subsided completely, some 6 weeks after the second admission. The patient was later discharged, continuing on appropriate doses of INAH, RMP, OFL, and EMB. He was subsequently seen at an outpatient clinic. Peritoneal fluid and sputum cultures for AFB were positive, the AFB being sensitive to INAH, RMP, EMB, and SM. Ofloxacin was then discontinued. Ethambutol was also discontinued 2 months after the successful re-introduction of RMP.

Discussion

Annual reports from the Chest Service of the Department of Health, Hong Kong, indicate that TB peritonitis is a very uncommon condition in Hong Kong (Table).[7] A high index of suspicion is required in order to reach the correct diagnosis, especially when there are relatively few gastrointestinal symptoms and signs, as seen in this case. Paracentesis for cell count and biochemistry aid in the initial diagnosis but are not considered to confirm the diagnosis.[3] Peritoneal fluid for AFB smears may be negative and culture for AFB takes several weeks. Laparoscopy with direct vision of the peritoneum, as well as tissue biopsy for histology, is recommended for confirmation of the diagnosis of TB peritonitis.[8]

Persistent fever after initial anti-TB treatment is a relatively common phenomenon.[9] In this patient, fever persisted for 6 weeks before total subsidence, causing great distress and concern for the patient and his family. Clinicians should persevere with anti-TB treatment after confirmation of the diagnosis. If other causes of fever have been excluded, and the fever persists for a lengthy period or becomes distressing, then a short course of prednisolone can be tried.[10] Potential liver toxicity due to anti-TB treatment requires close monitoring. If the hepatitis is severe, then all hepatotoxic anti-TB drugs must be temporarily discontinued and treatment changed to non-hepatotoxic anti-TB drugs such as SM, EMB, and OFL. When liver function returns to normal, the hepatotoxic drugs can be re-introduced one by one. Usually only one or two hepatotoxic drugs can be successfully re-introduced.[6,11]

Table. Tuberculosis notification in Hong Kong (1994-1998)

Year	Total number of cases of tuberculosis notified	Number of cases with tuberculous peritonitis No. (%)
1994	6319	18 (0.28)
1995	6212	13 (0.21)
1996	6501	11 (0.17)
1997	7072	13 (0.18)
1998	7673	8 (0.10)

Conclusion

TB peritonitis is an uncommon but significant presentation of tuberculosis. Importantly, it is not usually associated with pulmonary TB. It should certainly be considered in the differential diagnosis for patients presenting with lingering fever and abdominal symptoms of pain and swelling. Physicians should have a high index of suspicion for this entity, as early diagnosis and treatment reduces morbidity and mortality. Appropriate investigations, including laparoscopy and tissue biopsy, should be performed for patients strongly suspected of having the disease. Patients usually respond well to a conventional anti-TB treatment regimen. Potential complications of anti-TB medications, including liver function impairment, require monitoring. When indicated, appropriate modifications should be made to the treatment regimen, to optimise efficacy and minimise morbidity.

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